AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph on page 1, lines 7-8 to be as follows:

This application claims priority to U.S. Provisional Application Serial No. 60/140,477, filed June 22, 1999, the disclosure of which is explicitly incorporated by reference herein, and is a divisional application of U.S. Patent No. 6,706,519, filed on June 22, 2000.

Please amend the paragraph on page 5, lines 1-9 to be as follows:

Some of the present inventors have developed a microsystem platform and a micromanipulation device to manipulate said platform by rotation, thereby utilizing the centripetal forces resulting from rotation of the platform to motivate fluid movement through microchannels embedded in the microplatform, as disclosed in co-owned U.S. Patent No. 6,063,589, issued May 16, 2000, and co-owned and co-pending patent applications U.S. Serial Nos. 08/761,063, filed December 5, 1996; 08/768,990, filed December 18, 1996; 08/910,726, filed August 12, 1997; 08/995,056, filed December 19, 1997; 09/315,114, filed May 19, 1999; 09/579,492, filed May 12, 2000 and 09/~~___,___~~595,239, filed June 16, 2000 ~~(Attorney Docket No. 95-1408-XX)~~, the disclosures of each of which are explicitly incorporated by reference herein.

Please amend the paragraph on page 5, lines 13-18 to be as follows:

This invention provides Microsystems platforms as disclosed in co-owned U.S. Patent No. 6,063,589, issued May 16, 2000, and co-owned and co-pending patent applications U.S. Serial Nos. 08/761,063, filed December 5, 1996; 08/768,990, filed December 18, 1996; 08/910,726, filed August 12, 1997; 08/995,056, filed December 19, 1997; 09/315,114, filed May

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19, 1999; 09/579,492, filed May 12, 2000 and 09/___,___595,239, filed June 16, 2000 ~~(Attorney Docket No. 95-1408-XX)~~, the disclosures of each of which are explicitly incorporated by reference herein.

Please amend the paragraph on page 10, lines 5-16 to be as follows:

The platforms of the invention reduce the demands on automation in at least three ways. First, the need for precise metering of delivered fluids is relaxed through the use of on-disc metering structures, as described more fully in co-owned U.S. Patnet No. 6,063,589, issued May 16, 2000, and co-owned and co-pending patent applications U.S. Serial Nos. 08/761,063, filed December 5, 1996; 08/768,990, filed December 18, 1996; 08/910,726, filed August 12, 1997; 08/995,056, filed December 19, 1997; 09/315,114, filed May 19, 1999; 09/579,492, filed May 12, 2000 and 09/___,___595,239, filed June 16, 2000 ~~(Attorney Docket No. 95-1408-XX)~~, the disclosures of each of which are explicitly incorporated by reference herein. By loading imprecise volumes, slighting in excess of those needed for the assay, and allowing the rotation of the disc and use of appropriate microfluidic structures to meter the fluids, much simpler (and less expensive) fluid delivery technology may be employed than is the conventionally required for high-density microtitre plate assays.

Please amend the paragraph on page 13, lines 2-8 to be as follows:

This invention provides a microplatform and a micromanipulation device as disclosed in co-owned U.S. Patent No. 6,063,589, issued May 16, 2000, and co-owned and co-pending patent applications U.S. Serial Nos. 08/761,063, filed December 5, 1996; 08/768,990, filed December 18, 1996; 08/910,726, filed August 12, 1997; 08/995,056, filed December 19, 1997; 09/315,114,

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filed May 19, 1999; 09/579,492, filed May 12, 2000 and 09/___,___ 595,239, filed June 16, 2000 ~~(Attorney Docket No. 95-1408-XX)~~, the disclosures of each of which are explicitly incorporated by reference herein, adapted for performing microanalytical and microsynthetic assays of biological samples.

Please amend the paragraphs starting on page 13, line 16 and ending on page 14, line 2 to be as follows:

For the purposes of this invention, the term "a centripetally motivated fluid micromanipulation apparatus" is intended to include analytical centrifuges and rotors, microscale centrifugal separation apparatus, and most particularly the microsystems platforms and disk handling apparatuses as described in co-owned U.S. Patent No. 6,063,589, issued May 16, 2000, and co-owned and co-pending patent applications U.S. Serial Nos. 08/761,063, filed December 5, 1996; 08/768,990, filed December 18, 1996; 08/910,726, filed August 12, 1997; 08/995,056, filed December 19, 1997; 09/315,114, filed May 19, 1999; 09/579,492, filed May 12, 2000 and 09/___,___ 595,239, filed June 16, 2000 ~~(Attorney Docket No. 95-1408-XX)~~, the disclosures of each of which are explicitly incorporated by reference herein.

For the purposes of this invention, the term "microsystems platform" is intended to include centripetally-motivated microfluidics arrays as described in co-owned U.S. Patent No. 6,063,589, issued May 16, 2000, and co-owned and co-pending patent applications U.S. Serial Nos. 08/761,063, filed December 5, 1996; 08/768,990, filed December 18, 1996; 08/910,726, filed August 12, 1997; 08/995,056, filed December 19, 1997; 09/315,114, filed May 19, 1999; 09/579,492, filed May 12, 2000 and 09/___,___ 595,239, filed June 16, 2000 ~~(Attorney Docket~~

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~~No. 95-1408-XX~~), the disclosures of each of which are explicitly incorporated by reference herein.

Please amend the paragraph on page 17, lines 7-18 to be as follows:

The invention also comprises a micromanipulation device for manipulating the disks of the invention, wherein the disk is rotated within the device to provide centripetal force to effect fluid flow on the disk. Accordingly, the device provides means for rotating the disk at a controlled rotational velocity, for stopping and starting disk rotation, and advantageously for changing the direction of rotation of the disk. Both electromechanical means and control means, as further described herein, are provided as components of the devices of the invention. User interface means (such as a keypad and a display) are also provided, as further described in co-owned U.S. Patent No. 6,063,589, issued May 16, 2000, and co-owned and co-pending patent applications U.S. Serial Nos. 08/761,063, filed December 5, 1996; 08/768,990, filed December 18, 1996; 08/910726, filed August 12, 1997; 08/995,056, filed December 19, 1997; 09/315,114, filed May 19, 1999; 09/579,492, filed May 12, 2000 and 09/~~___,___~~595,239, filed June 16, 2000 ~~(Attorney Docket No. 95-1408-XX)~~, the disclosures of each of which are explicitly incorporated by reference herein.

Please amend the paragraph on page 18, lines 5-25 to be as follows:

In preferred embodiments, portions of the Microsystems platform surface are adapted for providing regions of controlled temperature (termed "thermal regions" or "thermal arrays" herein) using integral heating elements as disclosed in U.S. Patnet 6,063,589, incorporated by reference. In more preferred embodiments, the portions of the Microsystems platform surface

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are constituted in arrays of thermal control elements, most preferably wherein is produced adjacent regions of the platform surface having different temperatures. In preferred embodiments, the platform also comprises other components as disclosed in co-owned and co-pending patent applications U.S. Serial Nos. 08/761,063, filed December 5, 1996; 08/768,990, filed December 18, 1996; 08/910,726, filed August 12, 1997; 08/995,056, filed December 19, 1997; 09/315,114, filed May 19, 1999; 09/579,492, filed May 12, 2000 and 09/___,___595,239, filed June 16, 2000 ~~(Attorney Docket No. 95-1408-XX)~~, the disclosures of each of which are explicitly incorporated by reference herein, most preferably channels and microchannels, whereby fluid flow traverses each of the different regions having different temperatures at least once, or more preferably, several times. In these embodiments, the amount of time fluid is within any particular thermal region, and thus at any particular temperature is dependent on the path length of the channel in the region, the square of the hydraulic diameter of the channel, and the square of the rotational speed of the platform. In preferred embodiments, the arrays comprises at least 2 or 3 regions of different temperature adjacent to one another. In certain embodiments, the thermal regions are rectangular in shape, while in other embodiments, the thermal regions are wedge-shaped, having a broader annular diameter at positions distal to the axis of rotation than at positions proximal to the axis of rotation.

Please amend the paragraphs starting on page 19, line 15 and ending on page 20, line 15 to be as follows:

The invention provides a combination of specifically adapted microplatforms that are rotatable, analytic/synthetic microvolume assay platforms, and a micromanipulation device for manipulating the platform to achieve fluid movement on the platform arising from centripetal

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force on the platform as result of rotation. The platform of the invention is preferably and advantageously a circular disk; however, any platform capable of being rotated to impart centripetal for a fluid on the platform is intended to fall within the scope of the invention. The micromanipulation devices of the invention are more fully describe din co-owned and co-pending U.S. Serial Nos. U.S. Serial Nos. 08/761,063, filed December 5, 1996; 08/768,990, filed December 18, 1996; 08/910726, filed August 12, 1997; 08/995,056, filed December 19, 1997; 09/315,114, filed May 19, 1999; 09/579,492, filed May 12, 2000 and 09/___,___595,239, filed June 16, 2000 ~~(Attorney Docket No. 95-1408-XX)~~, the disclosures of each of which are explicitly incorporated by reference herein.

Fluid (including reagents, samples and other liquid components) movement is controlled by centripetal acceleration due to rotation of the platform. The magnitude of centripetal acceleration required for fluid to flow at a rate and under a pressure appropriate for a particular microfluidics structure on the Microsystems platform is determined by factors including but not limited to the effective radius of the platform, the interior diameter of microchannels, the position angle of the microchannels on the platform with respect to the direction of rotation, and the speed of rotation of the platform. In certain embodiments of the methods of the invention an unmetered amount of a fluid (either a sample or reagent solution) is applied to the platform and a metered amount is transferred from a fluid reservoir to a microchannel, as described in co-owned U.S. Patent No. 6,063,589, issued May 16, 2000, and co-owned and co-pending patent applications U.S. Serial Nos. 08/761,063, filed December 5, 1996; 08/768,990, filed December 18, 1996; 08/910726, filed August 12, 1997; 08/995,056, filed December 19, 1997; 09/315,114, filed May 19, 1999; 09/579,492, filed May 12, 2000 and 09/___,___595,239, filed June 16, 2000 ~~(Attorney Docket No. 95-1408-XX)~~, the disclosures of each of which are explicitly

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incorporated by reference herein. In preferred embodiments, the metered amount of the fluid sample provided on an inventive platform is from about 1nL to about 500μL. In these embodiments, metering manifolds comprising one or a multiplicity of metering capillaries are provided to distribute the fluid to a plurality of components of the microfluidics structure.

Please amend the paragraph starting on page 21 line 27 and ending on page 22 line17 to be as follows:

Platforms of the invention such as disks and the microfluidics components comprising such platforms are advantageously provided having a variety of composition and surface coatings appropriate for particular applications. Platform composition will be a function of structural requirements, manufacturing processes, and reagent compatibility/chemical resistance properties. Specifically, platforms are provided that are made from inorganic crystalline or amorphous materials, e.g., silicon, silica, quartz, inert metals, or from organic materials such as plastics, for example, poly(methyl methacrylate) (PMMA), acetonitrile-butadiene-styrene (ABS), polycarbonate, polyethylene, polystyrene, polyolefins, polypropylene and metallocene. These may be used with unmodified or modified surfaces as described below. The platforms may also be made from thermoset materials such as polyurethane and poly(dimethyl siloxane) (PDMS). Also provided by the invention are platforms made of composites or combinations of these materials; for example, platforms manufactures of a plastic material having embedded therein an optically transparent glass surface comprising detection chamber of the platform. Alternatively, platforms composed of layers made from different materials may be made. The surface properties of these materials may be modified for specific applications, as disclosed in co-owned U.S. Patent No. 6,063,589, issued May 16, 2000, and co-owned and co-pending patent

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applications U.S. Serial Nos. 08/761,063, filed December 5, 1996; 08/768,990, filed December 18, 1996; 08/910726, filed August 12, 1997; 08/995,056, filed December 19, 1997; 09/315,114, filed May 19, 1999; 09/579,492, filed May 12, 2000 and 09/~~___,___~~595,239, filed June 16, 2000 ~~(Attorney Docket No. 95-1408-XX)~~, the disclosures of each of which are explicitly incorporated by reference herein.

Please amend the paragraph starting on page 43 line 22 and ending on page 44 line 15 to be as follows:

In Figure 1, the disc 100 comprises at least three components: a microfluidics disc 201, a sealing layer 301, and one or more thermal sealing layers 401. In certain embodiments, microfluidics disc 201 is further provided as a combination of at least two component layers, wherein a reservoir layer 501 is bonded to a microfluidics layer 601. In these embodiments, the bottom face of the reservoir layer, when mated with the microfluidic layer described below, forms a complete network of enclosed channels and reservoirs through which fluids flow under the impetus of centripetal force created by rotation of the platform about a central axis. In all embodiments, fluid flow permits mixing of various component fluids in the assay and movement of the fluids from sample and reagent reservoirs through mixing structures and into assay collection chambers. In addition, fluid flow can be effectuated to include incubation and wash steps, suing structures disclosed in co-owned U.S. Patent No. 6,063,589, issued May 16, 2000 and incorporated by reference herein. Fluid flow rates of from about 1nL/s to about 1000μL/s are achieved at rotational speeds of from about 4 to about 30,000rpm. "Passive" or capillary valves are preferably used to control fluid flow in the platform as described in co-owned U.S. Patent No. 6,063,589, issued May 16, 2000, and co-owned and co-pending patent applications

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Please amend the paragraph on page 56 lines 1-9 to be as follows:

A microfluidics platform as depicted in Figures 1 through 4 was used to prepare and amplify a DNA target from samples of *E. coli*. Aspects of the instrument used for controlling the rotational profile and thermal cycling are described in co-owned U.S. Patent No. 6,063,589, issued May 16, 2000, and co-owned and co-pending patent applications U.S. Serial Nos. 08/761,063, filed December 5, 1996; 08/768,990, filed December 18, 1996; 08/910726, filed August 12, 1997; 08/995,056, filed December 19, 1997; 09/315,114, filed May 19, 1999; 09/579,492, filed May 12, 2000 and 09/~~___,___~~595,239, filed June 16, 2000 ~~(Attorney Docket No. 95-1408-XX)~~, the disclosures of each of which are explicitly incorporated by reference herein. The instrument used in this example is described above in the Detailed Description of Preferred Embodiments.

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